REMARKS

Claims 1-3 and 5-18 have been amended herein. Claims 1-3, 5-20, and 22-24 are currently pending and presented herein for reconsideration.

Claims 1-3, 6-7, 9-13, and 15-17 have been rejected under 35 U.S.C. § 101 as being directed to non-statutory subject matter. In accordance with the Examiner's suggestions, claims 1-3, 6-7, 9-13, and 15-17 have been amended in good-faith to be embodied in computer readable media without adding new matter to encompass statutory subject matter. Support for these amendments are exemplary set forth in Fig. 2 and paragraph [0060] of the specification. Accordingly, applicant respectfully requests that this rejection be withdrawn.

Claims 1-3, 5-20, and 22-24 have been rejected under 35 U.S.C. § 103 as being unpatentable over U.S. Published Patent Application No. 2002/0099302 to Bardy (hereinafter "Bardy") in view of U.S. Patent No. 5,978,751 to Pence et al. (hereinafter "Pence"). Applicant respectfully traverses this rejection.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q. 2d 1438 (Fed. Cir. 1991); MPEP 2143. Here, the Examiner has failed to establish a *prima facie* case of obviousness because Bardy and Pence independently or in combination do not teach or suggest all the claim limitations of claim 1-3, 5-20, and 22-24.

Applicant respectfully submits neither Bardy nor Pence is even remotely concerned with analyzing clinical trail data, let alone continuously analyzing trial data of an ongoing blinded clinical trial for a statistically significant event to identify a potential positive or negative effect of a drug under study at the earliest possible moment without suspending the ongoing blinded clinical trial, as required by claims 1-3, 5-20, and 22-24. It is well established that the Examiner cannot use hindsight gleaned from the claimed invention to modify or reconstruct the prior art reference to render claims unpatentable.

It is unclear to applicant as to why Bardy is relevant as a prior art reference, let alone as a primary reference, when Bardy fails to teach or suggest any of the claimed steps of claim 1 (and similarly for independent claims 12 and 18). Further, it is unclear to applicant why Pence is relevant as a prior art reference when Pence relates to a manufacturing method and system for testing magnetic disk drives. The prior must to be judged based on a full and fair consideration of what that art teaches, not by using applicant's invention as a blueprint for gathering various bits and modifying the pieces in an attempt to reconstruct applicant's invention. The Examiner cannot simply change the principle of the operation of the reference or render the reference inoperable for its intended purpose to render the claims unpatentable. Accordingly, it is submitted that the Examiner has succumbed to the lure of prohibited hindsight reconstruction.

Applicant once again submits that the only the claimed invention teach or suggest a method and system of continuously analyzing trial data of an ongoing blinded clinical trial utilizing multi-arm study without suspending and compromising the integrity of the ongoing blinded clinical trial. None of the prior art teaches such analysis while the blinded clinical trial is still ongoing because of the fear of compromising the integrity the trial data and thereby jeopardizing the veracity of the blinded clinical trials. The ongoing blinded clinical trial can be compromised if the source of the data is revealed or can be determined (i.e., the trial data is associated with a particular study arm). Millions of dollars spent on clinical trials can be wasted if the integrity of the blinded clinical trials is compromised. All of the prior art systems and methods describe analyzing the trial data

only after the clinical trials have ended. (*See, e.g.*, Specification at ¶ [0013]). That is, under the prior art system and method, potential positive or negative effects of a drug under study will go unnoticed until the clinical trial is completed. The present system and method continuously analyzes the trial data for a statistically significant event to identify a potential positive or negative effect of a drug under study at the earliest possible moment without suspending and compromising the integrity of the ongoing blinded clinical trial. A statistically significant event occurs when the result of the statistical analysis exceeds a predetermined threshold. For example, if the drug under study has a high toxicity level, then it would be extremely valuable to identify such negative effect of the drug as earliest possible to end the clinical trial. Only the claimed invention teaches or suggests identifying such potential positive or negative effects while the blinded clinical is ongoing without compromising the integrity and the blindness of the clinical trial. Because of this and other advantages of the claimed invention, the assignee of the present application is currently marketing and selling products/services incorporating various embodiments of the claimed invention with great success.

Whereas, Bardy relates to a system and method for diagnosing and monitoring congestive heart failure in a patient and Pence relates to a manufacturing method and system for testing magnetic disk drives. Applicants respectfully submit that neither Bardy nor Pence is not even remotely related to clinical trials and is not concerned with maintaining the secrecy of the collected data. In fact, Bardy must know the source of the data to determine if the patient will or is experiencing congestive heart failure and Pence must know the source of the data to determine which manufacturing station is cause of the device failures.

Accordingly, applicant respectfully submits that the combination of Bardy and Pence fails to cure the aforenoted deficiencies of the prior art systems. That is, even assuming *arguendo* that Bardy and Pence relate to a system for analyzing clinical trial data, as with the prior art system in the background section of the specification, the combination of Bardy and Pence fails to teach or suggest accessing and analyzing clinical

trial data of an ongoing blinded clinical trial without suspending and compromising the integrity of the ongoing blinded clinical trail, as required in claims 1-3, 5-20 and 22-24.

"To imbue one of ordinary skill in the art with knowledge of the present invention, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim of the insidious effect of hindsight syndrome, wherein that which only the inventor taught is used against the teacher." W.L. Gore & Assoc. v. Garlock, Inc., 721 F.2d 1540, 1553 (Fed. Cir. 1983). In the present case, none of the references teach or suggest continuously analyzing trial data of an ongoing blinded clinical trial for a statistically significant event to identify a potential positive or negative effect of a drug under study at the earliest possible moment without suspending and compromising the integrity of the ongoing blinded clinical trial, as required by claims 1-3, 5-20, and 22-24.

Contrary to the Examiner's assertion, applicant respectfully submits that Bardy or Pence independently or in combination fail to teach or suggest many of the claimed limitations in independent claim 1 (and similarly for independent claims 12 and 18).

I. Bardy and Pence Fails to Teach or Suggest Accessing a Trial Database Comprising Trial Data of Subjects in an Ongoing Blinded Clinical Trial Comprising a Multi-arm Study Without Comprising Integrity of the Ongoing Blinded Clinical Trial

As noted herein, Bardy relates to a system and method for diagnosing and monitoring congestive heart failure in a patient and Pence relates to a manufacturing method and system for testing magnetic disk drives. Both Bardy and Pence teaches away from the claimed invention because they must know the data source (i.e., the identity of the patient or defective magnetic disk drive). Even after acknowledging that neither Bardy nor Pence is even remotely relate to clinical trials, the Examiner continues to assert that Bardy discloses accessing a trial database comprising trial data of subjects in an ongoing blinded clinical trial comprising a multi-arm study without compromising integrity of the ongoing blinded clinical trial. (*See* Office Action at 5, 11 and 15). In fact, paragraphs [0008], [0009] in Bardy, cited by the Examiner, merely describes

accessing patient care records. Contrary to the Examiner's assertion, Bardy does not even remotely suggest or teach accessing a trial database, let alone accessing a trial database of an ongoing blinded clinical trial where the data must be accessed without compromising the integrity of the blind. That is, the clinical trial data must be accessed without revealing the source of the data (i.e., the data must be accessed without knowing that it relates to a particular patient). Whereas, contrary to the Examiner's assertion, Bardy clearly teaches away from the claimed invention because the source of the data must be known to provide proper care to the patient:

> "The present invention provides a system and method for diagnosing and monitoring the onset, progression, regression, and status quo of congestive heart failing using an automated collection and analysis patient care system ... The measures are collected on a regular, periodic basis for storage in a database along with other patient care records." (Bardy, ¶ [0009]).

After careful reading of Bardy, applicant is unable to find any reference to blinded clinical trial, let alone clinical trial database. Applicant respectfully requests that the Examiner identify where in Bardy it allegedly teaches "accessing a trial database comprising trial data of subjects in an ongoing blinded clinical trial comprising a multi-arm study without compromising integrity of the ongoing blinded clinical trial," as required in independent claim 1 (and similarly in independent claims 12 and 18).

Additionally, in response to applicant's amendment filed on October 2, 2008, the Examiner cites paragraph [0008] of the specification and appears to incorrectly assert that accessing a trial database comprising trial data of subjects in an ongoing blinded clinical trial comprising a multi-arm study is known in the art as allegedly admitted by applicant's own admission. That is, the Examiner still appears to completely misunderstand the claimed invention.

Contrary to the Examiner's assertion, applicant's claimed invention is not the blinded clinical trial but comprises "accessing a trial database comprising trial data of

subjects in an ongoing blinded clinical trial comprising a multi-arm study without compromising integrity of the ongoing blinded clinical trial," as required in independent claim 1 (and similarly in independent claims 12 and 18). In this regard, applicant kindly directs the Examiner's attention various paragraphs of the specification wherein applicant's discusses prior art's inability to access and analysis the clinical trial data until the end of the trial (i.e., NOT DURING THE ONGOING BLINDED CLINICAL TRIAL):

> "Generally, at the end of the trial, the database containing the completed trial data is shipped to a statistician for analysis." (emphasis added) (Specification at ¶ [0009]).
>
> "Unfortunately, because the study arm assignments are blinded, there is no way to separate out subjects and their data into corresponding groups for purposes of performing comparisons while the trial is being conducted. Since many clinical trials may last for time periods extending for years, it is conceivable to have a treatment toxicity go unnoticed for prolonged periods without intervention." (emphasis added) (Specification at ¶ [0012]).
>
> "At present, when clinical trials are randomized and blinded, identification of a particularly effective treatment may not be realized until the entire clinical trial is completed." (emphasis added) (Specification at ¶ [0014]).
>
> "In a case where the study data reaches statistical significance, as accrual of subjects continues, and data is received, an optimal time to close a clinical study would be at the very moment when statistical significance is achieved. While that moment may arrive earlier in the course of a clinical trial, there is no way of knowing this, and therefore time and money are lost." (Specification at ¶ [0016]).
>
> "In spite of the latest technological advancements made in the area of data collection through electronic systems, there is still a disadvantage in that it is very difficult to draw conclusions about a medical treatment while the data is being collected during the trial. This limitation stems primarily from the fact that statistical analysis cannot begin until the trial data has been fully cleaned and processed." (emphasis added) (Specification at ¶ [0033]).

Accordingly, the object of the claimed invention is to provide:

> Therefore, it is desirable to provide a method and system for conducting statistical analysis on the clinical data collected while the trial is ongoing. (emphasis added) (Specification at ¶ [0035).
>
> In the case of a randomized clinical trial where maintaining confidentiality is important, it is also desirable to provide a secure system in which the blinding information is integrated in such a way that the clinical trial data and blinding data are stored securely to prevent users from accessing the data and yet allow the execution of programs for performing statistical comparisons between study arms while the trial is ongoing. (emphasis added) (Specification at ¶ [0036).

Therefore, the Examiner has failed to establish a *prima facie* case of obviousness because the combination of Bardy and Pence does not teach or suggest the claimed limitation of "accessing a trial database comprising trial data of subjects in an ongoing blinded clinical trial comprising a multi-arm study without compromising integrity of the ongoing blinded clinical trial," as required in independent claim 1 (and similarly in independent claims 12 and 18) and included in dependent claims 2-3, 5-11, 13-17, 19-20 and 22-24. Contrary to the Examiner's assertion, applicant alleged own admission does not cure these fatal deficiencies of Bardy and Pence because they do not teach or suggest analyzing the clinical data of an ongoing blinded clinical trial without suspending and compromising the integrity of the ongoing blinded clinical trial. The prior must to be judged based on a full and fair consideration of what that art teaches, not by using applicant's invention as a blueprint for gathering various bits and modifying the pieces in an attempt to reconstruct Applicant's invention. The Examiner cannot simply contradict and/or modify the clear teaching of the reference to render the claims unpatentable.

II. Bardy and Pence Fails to Teach or Suggest Accessing a Blinding Database Comprising Subject Identifiers and Associated Study Group Identifiers Without Comprising the Integrity of the Ongoing Blinded Clinical Trial

As noted herein, Bardy relates to a system and method for diagnosing and monitoring congestive heart failure in a patient and Pence relates to a manufacturing

method and system for testing magnetic disk drives. Both Bardy and Pence teaches away from the claimed invention because they must know the data source (i.e., the identity of the patient or defective magnetic disk drive). However, the Examiner continues to assert that Bardy discloses accessing a blinding database comprising subject identifiers and associated study group identifiers without compromising the integrity of the blinded clinical trial, wherein a subject's study group identifiable by a study group identifier. (*See* Office Action at 6, 12 and 15). In fact, paragraph [0011] in Bardy, cited by the Examiner, merely describes that "[e]ach monitoring set includes recorded measures that each relates to patient information." (Emphasis added). Further, paragraph [0037] in Bardy, cited by the Examiner, merely describes "continuously and periodically [collecting patient's cardiovascular measurements] as part of on-going patient care monitoring." (Emphasis added).

Contrary to the Examiner's assertion, Bardy does not even remotely suggest or teach accessing a trial database, let alone accessing a blinding database where the data must be accessed without compromising the integrity of the blind. That is, the clinical trial data must be accessed without revealing the source of the data (i.e., the data must be accessed without knowing that it relates to a particular patient). Whereas, contrary to the Examiner's assertion, Bardy clearly teaches away from the claimed invention because Bardy cannot provide proper care to a patient unless it has access to the patient's medical data. Once again, after careful reading of Bardy, applicant is unable to find any reference to a blinding database, let alone clinical trial database. Applicant respectfully requests that the Examiner identify where in Bardy it allegedly teaches "accessing a blinding database comprising subject identifiers and associated study group identifiers without compromising the integrity of the ongoing blinded clinical trial, wherein a subject's study group identifiable by a study group identifier," as required in independent claim 1 (and similarly in independent claims 12 and 18).

As noted herein, applicant's claimed invention is not the blinded clinical trial but comprises "accessing a blinding database comprising subject identifiers and associated

study group identifiers without compromising the integrity of the ongoing blinded clinical trial, wherein a subject's study group identifiable by a study group identifier," as required in independent claim 1 (and similarly in independent claims 12 and 18).

Therefore, the Examiner has failed to establish a *prima facie* case of obviousness because the combination of Bardy and Pence does not teach or suggest the claimed limitation of "accessing a blinding database comprising subject identifiers and associated study group identifiers without compromising the integrity of the ongoing blinded clinical trial, wherein a subject's study group identifiable by a study group identifier," as required in independent claim 1 (and similarly in independent claims 12 and 18) and included in dependent claims 2-3, 5-11, 13-17, 19-20 and 22-24. Contrary to the Examiner's assertion, applicant alleged own admission does not cure these fatal deficiencies of Bardy and Pence because they do not teach or suggest analyzing the clinical data of an ongoing blinded clinical trial without suspending and compromising the integrity of the ongoing blinded clinical trial. The prior must to be judged based on a full and fair consideration of what that art teaches, not by using applicant's invention as a blueprint for gathering various bits and modifying the pieces in an attempt to reconstruct Applicant's invention. The Examiner cannot simply contradict and/or modify the clear teaching of the reference to render the claims unpatentable.

III. Bardy and Pence Fails to Teach or Suggest Generating a Grouped Database From the Trial Database and the Blinding Database Without Compromising the Integrity of the Ongoing Blinded Clinical Trial

As noted herein, Bardy relates to a system and method for diagnosing and monitoring congestive heart failure in a patient and Pence relates to a manufacturing method and system for testing magnetic disk drives. Both Bardy and Pence teaches away from the claimed invention because they must know the data source (i.e., the identity of the patient or defective magnetic disk drive). However, the Examiner continuous to assert that Bardy discloses generating a grouped database from the trial database and the

blinding database for statistical analysis without compromising the integrity of the ongoing blinded clinical trial. (*See* Office Action at 6, 12 and 15). In fact, paragraph [0035] in Bardy, cited by the Examiner, merely describes that

> "The database 17 stores patient care records 23 for each individual patient to whom remote patient care is being provided. Each patient care record 23 contains normal patient identification and treatment profile information, as well as medical history, medications taken, height and weight, and other pertinent data."

Contrary to the Examiner's assertion, Bardy does not even remotely suggest or teach a trial or blinding database, let alone generating a grouped database from the trial and blinding databases without compromising the integrity of the ongoing blinded clinical trial. Applicant respectfully submits that neither Bardy nor Pence teach or suggest generating a grouped database because neither is concerned with multi-arm study to determine the efficacy of a particular drug vs. another drug or placebo. Once again, after careful reading of Bardy, applicant is unable to find any reference to a trial or blinding database, let alone a grouped database. Applicant respectfully requests that the Examiner identify where in Bardy it allegedly teaches "generating a grouped database from the trial database and the blinding database for statistical analysis without compromising the integrity of the ongoing blinded clinical trial," as required in independent claim 1 (and similarly in independent claims 12 and 18).

As noted herein, applicant's claimed invention is not the blinded clinical trial but comprises "generating a grouped database from the trial database and the blinding database for statistical analysis without compromising the integrity of the ongoing blinded clinical trial," as required in independent claim 1 (and similarly in independent claims 12 and 18).

Therefore, the Examiner has failed to establish a *prima facie* case of obviousness because the combination of Bardy and Pence does not teach or suggest the claimed limitation of "generating a grouped database from the trial database and the blinding

database for statistical analysis without compromising the integrity of the ongoing blinded clinical trial," as required in independent claim 1 (and similarly in independent claims 12 and 18) and included in dependent claims 2-3, 5-11, 13-17, 19-20 and 22-24. Contrary to the Examiner's assertion, applicant alleged own admission does not cure these fatal deficiencies of Bardy and Pence because they do not teach or suggest analyzing the clinical data of an ongoing blinded clinical trial without suspending and compromising the integrity of the ongoing blinded clinical trial. The prior must to be judged based on a full and fair consideration of what that art teaches, not by using applicant's invention as a blueprint for gathering various bits and modifying the pieces in an attempt to reconstruct Applicant's invention. The Examiner cannot simply contradict and/or modify the clear teaching of the reference to render the claims unpatentable.

IV. Bardy and Pence Fails to Teach or Suggest Performing a Statistical Analysis on the Accessed Trial Database Without Suspending and Compromising the Integrity of the Ongoing Blinded Clinical Trial

As noted herein, Bardy relates to a system and method for diagnosing and monitoring congestive heart failure in a patient and Pence relates to a manufacturing method and system for testing magnetic disk drives. Both Bardy and Pence teaches away from the claimed invention because they must know the data source (i.e., the identity of the patient or defective magnetic disk drive). However, the Examiner continues to assert that Bardy discloses performing a statistical analysis on the accessed trial database without suspending and compromising the integrity of the ongoing blinded clinical trial. (*See* Office Action at 6, 11 and 15). In fact, paragraph [0009] in Bardy, cited by the Examiner, merely describes that

> "The measures are collected on a regular, periodic basis for storage in a database along with other patient care records. Derived measures are developed from the stored measures. Select stored and derived measures are analyzed and changes in patient condition are logged."

In the claimed invention, it is critical that the integrity of the blind is maintained. That is, the operator/user cannot know or determine that the accessed data is associated with a particular clinical trial participant or a study group. Accordingly, the claimed invention requires that the statistical analysis be performed while maintaining the integrity of the blind and without suspending the ongoing blinded clinical trial. However, Bardy teaches away from the claimed invention because the operator/user of the Bardy system must know that the accessed data is associated with a particular patient to properly analyze the patient's condition. That is, even assuming *arguendo* that Bardy relates to a clinical trial, Bardy cannot provide proper care to the patient without compromising the integrity of the blind. Hence, contrary to the Examiner's erroneous assertion, applicant respectfully submits that Bardy fails to teach or suggest "performing a statistical analysis on the accessed trial database without suspending and compromising the integrity of the ongoing blinded clinical trial," as required in independent claim 1 (and similarly in independent claims 12 and 18), because Bardy must compromise the integrity of the blind to access and analyze the medical data of a particular patient to provide proper medical care.

Further, Bardy describes that derived measures are calculated from the stored measures, e.g., calories burned can be derived from patient's walk if the speed and duration of the walk is known. One of ordinary skill in the art would not equate derived measures with performing statistical analysis as suggested by the Examiner.

As noted herein, applicant's claimed invention is not the blinded clinical trial but comprises "performing a statistical analysis on the accessed trial database without suspending and compromising the integrity of the ongoing blinded clinical trial," as required in independent claim 1 (and similarly in independent claims 12 and 18).

Therefore, the Examiner has failed to establish a *prima facie* case of obviousness because the combination of Bardy and Pence does not teach or suggest the claimed limitation of "performing a statistical analysis on the accessed trial database without

suspending and compromising the integrity of the ongoing blinded clinical trial," as required in independent claim 1 (and similarly in independent claims 12 and 18) and included in dependent claims 2-3, 5-11, 13-17, 19-20 and 22-24. Contrary to the Examiner's assertion, applicant alleged own admission does not cure these fatal deficiencies of Bardy and Pence because they do not teach or suggest analyzing the clinical data of an ongoing blinded clinical trial without suspending and compromising the integrity of the ongoing blinded clinical trial. The prior must to be judged based on a full and fair consideration of what that art teaches, not by using applicant's invention as a blueprint for gathering various bits and modifying the pieces in an attempt to reconstruct Applicant's invention. The Examiner cannot simply contradict and/or modify the clear teaching of the reference to render the claims unpatentable.

V. Bardy and Pence Fails to Teach or Suggest Determining Whether the Result of the Statistical Analysis Exceeds a Predetermined Threshold Value

As noted herein, Bardy relates to a system and method for diagnosing and monitoring congestive heart failure in a patient and Pence relates to a manufacturing method and system for testing magnetic disk drives. However, the Examiner continues to assert that Bardy discloses determining whether the result of the statistical analysis exceeds a predetermined threshold value. (*See* Office Action at 6, 12 and 15). In fact, paragraph [0059] in Bardy, cited by the Examiner, merely describes using a standard statistical linear regression technique involving a least squares error fit to perform the threshold tests. One of ordinary skill in the art would not equate performing the threshold tests with performing statistical analysis on the accessed trial database without compromising the integrity of the blind and suspending the ongoing blinded clinical trial and then comparing the result of the statistical analysis to a predetermined threshold value. As noted herein, it is critical that the integrity of the blind is maintained in the claimed invention. That is, the operator/user cannot know or determine that the accessed data is associated with a particular clinical trial participant or a study group.

Accordingly, the claimed invention requires that the statistical analysis be performed while maintaining the integrity of the blind and without suspending the ongoing blinded clinical trial. However, contrary to the Examiner's assertion, Bardy teaches away from the claimed invention because the operator/user of the Bardy system must know that the accessed data is associated with a particular patient to properly analyze the patient's condition. That is, even assuming *arguendo* that Bardy relates to a clinical trial, Bardy cannot provide proper care to the patient without compromising the integrity of the blind. Hence, contrary to the Examiner's erroneous assertion, applicant respectfully submits that Bardy fails to teach or suggest "determining whether the result of the statistical analysis exceeds a predetermined threshold value," as required in independent claim 1 (and similarly in independent claims 12 and 18), because Bardy must compromise the integrity of the blind to access and analyze the medical data of a particular patient to provide proper medical care.

Therefore, the Examiner has failed to establish a *prima facie* case of obviousness because the combination of Bardy and Pence does not teach or suggest the claimed limitation of "determining whether the result of the statistical analysis exceeds a predetermined threshold value," as required in independent claim 1 (and similarly in independent claims 12 and 18) and included in dependent claims 2-3, 5-11, 13-17, 19-20 and 22-24.

Moreover, since neither Bardy nor Pence remotely relates to a clinical trial, neither reference is suggestive of performing statistical analysis for a statistically significant event to identify a potential positive or negative effect of a drug under study at the impermissibly earliest possible moment while maintaining the blindness of the clinical trial. The prior must to be judged based on a full and fair consideration of what that art teaches, not by using applicant's invention as a blueprint for gathering various bits and modifying the pieces in an attempt to reconstruct Applicant's invention. It is well established that the Examiner cannot use hindsight gleaned from the claimed invention to modify or reconstruct the prior art reference to render claims unpatentable.

VI. Bardy and Pence Fails to Teach or Suggest Repeating the Steps of Accessing, Performing and Determining While the Blinded Clinical Trial is Ongoing Without Compromising the Integrity of the Ongoing Blinded Clinical Trial

As noted herein, Bardy relates to a system and method for diagnosing and monitoring congestive heart failure in a patient. Accordingly, the Examiner admits that Bardy is not suggestive of this repeating step and turns to Pence for allegedly describing this repeating step. However, as noted herein, Pence relates to a manufacturing method and system for testing magnetic disk drives. Since Bardy and Pence does not remotely relate to a clinical trial, neither is suggestive of repeating the steps of accessing the trial database, performing statistical analysis, and determining whether the result of the statistical analysis exceeds the predetermined threshold value without compromising the integrity of the ongoing blinded clinical trial without compromising the integrity of the ongoing blinded clinical trial if it is determined that the result of the statistical analysis does not exceed the predetermined threshold. Additionally, both Bardy and Pence teaches away from the claimed invention because they must know the data source (i.e., the identity of the patient or defective magnetic disk drive). It is well established that the Examiner cannot use hindsight gleaned from the claimed invention to impermissibly modify or reconstruct the prior art reference to render claims unpatentable.

Nevertheless, the Examiner continues to assert that Pence discloses if repeating the steps of accessing the trial database, performing statistical analysis, and determining whether the result of the statistical analysis exceeds the predetermined threshold value without compromising the integrity of the ongoing blinded clinical trial without compromising the integrity of the ongoing blinded clinical trial if it is determined that the result of the statistical analysis does not exceed the predetermined threshold. (*See* Office Action at 6, 12 and 15-16). In fact, col. 5, lines 30-46 in Pence, cited by the Examiner, merely describes that for each input, a determination is made whether or not the input record is valid. One of ordinary skill in the art would not equate determining if the input record is valid for each input with repeating the steps of accessing the trial database,

performing statistical analysis, and determining whether the result of the statistical analysis exceeds the predetermined threshold value without compromising the integrity of the ongoing blinded clinical trial, as apparently suggested by the Examiner.

As noted herein, it is critical that the integrity of the blind is maintained in the claimed invention. That is, the operator/user cannot know or determine that the accessed data is associated with a particular clinical trial participant or a study group. Accordingly, the claimed invention requires that the statistical analysis be performed while maintaining the integrity of the blind and without suspending the ongoing blinded clinical trial. However, both Bardy and Pence teach away from the claimed invention because the operator/user must know that the accessed data is associated with a particular patient so Bardy can properly analyze the patient's condition and must know that the input record is associated with particular disk drive so Pence can determine if the disk drive is defective in Pence. That is, even assuming *arguendo* that Bardy and Pence relate to a clinical trial, Bardy cannot provide proper care to the patient and Pence cannot determine if the disk drive is defective without compromising the integrity of the blind. Hence, contrary to the Examiner's erroneous assertion, applicant respectfully submits that the combination of Bardy and Pence fails to teach or suggest repeating the steps of accessing the trial database, performing statistical analysis, and determining whether the result of the statistical analysis exceeds the predetermined threshold value without compromising the integrity of the ongoing blinded clinical trial if it is determined that the result of the statistical analysis does not exceed the predetermined threshold, as required in independent claim 1 (and similarly in independent claims 12 and 18).

Therefore, the Examiner has failed to establish a *prima facie* case of obviousness because the combination of Bardy and Pence does not teach or suggest the claimed limitation of repeating the steps of accessing the trial database, performing statistical analysis, and determining whether the result of the statistical analysis exceeds the predetermined threshold value without compromising the integrity of the ongoing blinded clinical trial if it is determined that the result of the statistical analysis does not exceed the

predetermined threshold, as required in independent claim 1 (and similarly in independent claims 12 and 18) and included in dependent claims 2-3, 5-11, 13-17, 19-20 and 22-24. Contrary to the Examiner's assertion, applicant alleged own admission does not cure these fatal deficiencies of Bardy and Pence because they do not teach or suggest analyzing the clinical data of an ongoing blinded clinical trial without suspending and compromising the integrity of the ongoing blinded clinical trial. The prior must to be judged based on a full and fair consideration of what that art teaches, not by using applicant's invention as a blueprint for gathering various bits and modifying the pieces in an attempt to reconstruct Applicant's invention. The Examiner cannot simply contradict and/or modify the clear teaching of the reference to render the claims unpatentable.

Not only does Bardy and Pence independently or in combination fail to teach or suggest continuously analyzing trial data of an ongoing blinded clinical trial for a statistically significant event to identify a potential positive or negative effect of a drug under study, as required by claims 1-3, 5-20, and 22-24. The combination of Bardy and Pence fails to teach or suggest many of the claimed steps of accessing a trial database, accessing a blinding database, generating a grouped database, performing a statistical analysis, determining, and repeating, as required in independent claim 1 (and similarly in independent claims 12 and 18). Hence, applicants respectfully submit that the Examiner has failed to establish the basic requirements of a *prima facie* case of obviousness for claims 1-3, 5-20, and 22-24.

VII. Bardy and Pence Fails to Solve the Problem of Analyzing Clinical Trial Data of Ongoing Blinded Clinical Trial Without Suspending and Compromising the Integrity of the Ongoing Blinded Clinical Trial

Further, the claimed invention defined by the claims eliminates the shortcomings and disadvantages encountered with the prior art. Specifically, the claimed invention continuously analyzes trial data of an ongoing blinded clinical trial for a statistically significant event to identify a potential positive or negative effect of a drug under study

without suspending and compromising the integrity of the ongoing blinded clinical trial. None of the cited references are directed to the problem solved by the claimed invention. It is undeniable that neither Bardy nor Pence is even remotely concerned with the problem of continuously analyzing trial data of an ongoing blinded clinical trial for a statistically significant event to identify a potential positive or negative effect of a drug under study at the earliest possible moment without suspending and compromising the integrity of the ongoing blinded clinical trial. The mere fact that the prior art can be modified does not make the modification obvious. Here, as noted herein, the Examiner's primary reference (Bardy) relates to solving a completely different problem of diagnosing and monitoring congestive hear failure in a patient; and the secondary reference (Pence) relates to solving another completely different and non-related problem of providing manufacturing system and method for testing devices, such as magnetic disk drives. In fact, both Bardy and Pence teaches away from the claimed invention because they must know the data source (i.e., the identity of the patient or defective magnetic disk drive, thereby compromising the integrity of the blind).

Absent evidence that the specific problem of continuously analyzing trial data of an ongoing blinded clinical trial for a statistically significant event to identify a potential positive or negative effect of a drug under study without suspending and compromising the integrity of the ongoing blinded clinical trial was even recognized by the prior art, there can be no finding that the invention as a whole would have been obvious. As stated by the PTO Board of Appeals in Ex parte Breidt and Lefevre, 161 U.S.P.Q. 767, 768 (1968), "an inventive contribution can reside as well in the recognition of a problem as in a solution". It further appears that the conclusion reached by the Board of Appeals in Ex parte Minks, 169 U.S.P.Q. 120 (1969), is here in point. There, the Board concluded that "[a]ppellant having discovered the source of the problem and solved the same ... he is ... entitled to patent protection". Id. at 121.

Since applicant has recognized a problem not addressed by the cited prior art and solved that problem in a manner not suggested by either Bardy or Pence, the basis for

patentability of the claims is established. See In re Wright, 6 U.S.P.Q. 2d, 1959, 1961-1962 (Fed. Cir. 1988). There, the CAFC relied upon previous decisions requiring a consideration of the problem facing the inventor in reversing the Examiner's rejection. "The problem solved by the invention is always relevant". Id. at 1962. See also, In re Rinehart, 189 U.S.P.Q. 143, 149 (C.C.P.A. 1967), which stated that the particular problem facing the inventor must be considered in determining obviousness.

VIII. DEPENDENT CLAIMS:

Contrary to the Examiner's assertion, applicant submits that only the claimed invention teaches or suggests "reading a user defined criteria that defines the level of cleanliness of the trial data for statistical analysis; and retrieving only those trial data that meet the user defined criteria from the trial database," as required in claims 2, 7, and 13. In fact, paragraph [0048] in Bardy, cited by the Examiner, merely describes comparing the measured values to a stored a set of indicator thresholds and quality of life and symptom measures set to the reference baseline. One of ordinary skill in the art would not equate such comparisons with the level of cleanliness of the trial data for statistical analysis, as erroneously suggested by the Examiner. Further, paragraph [0011] in Bardy, cited by the Examiner, merely describes that a plurality of monitoring sets is retrieved from a database. Once again, one of ordinary skill in the art would not equate such retrieving a monitoring set from the database with retrieving trial data that meet user defined level of cleanliness, as erroneously suggested by the Examiner. Moreover, after careful reading of Bardy, applicant is unable to find any reference to clinical trial data, let alone cleanliness of the trial data. Applicant respectfully requests that the Examiner identify where in Bardy it allegedly teaches "reading a user defined criteria that defines the level of cleanliness of the trial data for statistical analysis; and retrieving only those trial data that meet the user defined criteria from the trial database," as required in claims 2, 7, and 13. The Examiner cannot simply change the principle of the operation of the reference or render the reference inoperable for its intended purpose to render the claims unpatentable.

Claim 3 additionally requires "waiting for a predetermined time period prior to the repeating step if it is determined that the result of the statistical analysis does not exceed the predetermined threshold value." In fact, col. 5, lines 47-51 in Pence, cited by the Examiner, merely describes a system waiting for an input. One of ordinary skill in the art would not equate a system waiting for input with waiting for a predetermined time period prior to the repeating step if it is determined that the result of the statistical analysis does not exceed the predetermined threshold value, as erroneously suggested by the Examiner. Applicant respectfully requests that the Examiner identify where in Pence it allegedly teaches "waiting for a predetermined time period prior to the repeating step if it is determined that the result of the statistical analysis does not exceed the predetermined threshold value," as required in claim 3. The Examiner cannot simply change the principle of the operation of the reference or render the reference inoperable for its intended purpose to render the claims unpatentable.

Claim 5 (and similarly claims 8, 14, and 22) additionally require "storing the grouped database in a memory device that is inaccessible by any user." In fact, col. 5, lines 47-51 in Pence, cited by the Examiner, merely describes

> "As a further description of the unit history record mentioned above, a single record is stored in a database on disk 11 of FIG. 1 for each disk drive or device. There is keyed access to this record, based on unique device serial number."

One of ordinary skill in the art would not equate providing keyed access to the record with storing the grouped database in a memory device that is inaccessible by an user, as erroneously suggested by the Examiner. Moreover, after careful reading of Pence, applicant is unable to find any reference to clinical trial database, let alone a grouped database, which is generated from the trial and blinding databases. Applicant respectfully requests that the Examiner identify where in Bardy or Pence it allegedly teaches "storing the grouped database in a memory device that is inaccessible by any user," as required in claims 5 (and similarly in claims 8, 14, and 22). The Examiner cannot simply change the

principle of the operation of the reference or render the reference inoperable for its intended purpose to render the claims unpatentable.

Claims 6, 15, and 23 additionally require performing a "statistical analysis without locking the trial database." As noted herein, neither Bardy nor Pence teaches or suggests clinical trial, let alone statistically analyzing the trial data of an ongoing blinded clinical trial. Further, as noted herein, the combination of Bardy and Pence teaches away from the claimed invention because both Bardy and Pence cannot access the data without compromising the integrity of the blind (i.e., the source of the data). That is, only the claimed invention teaches accessing a clinical trial database without compromising the integrity of the blind and without locking the trial database. The Examiner cannot simply change the principle of the operation of the reference or render the reference inoperable for its intended purpose to render the claims unpatentable.

Claims 9, 16, and 24 additionally require alerting "a user if it is determined that the result of the statistical analysis exceeds the predetermined threshold value." As noted herein, neither Bardy nor Pence teaches or suggests performing statistical analysis on trial data of an blinded clinical trial, let alone alerting the user if the result of the statistical analysis exceeds the predetermined threshold. In fact, item 127 of Fig. 5 in Bardy, cited by the Examiner, merely describes a patient status indicator. The Examiner cannot simply change the principle of the operation of the reference or render the reference inoperable for its intended purpose to render the claims unpatentable.

Claim 11 additionally requires "retrieving a user defined statistical model; and running the retrieved user defined statistical model on the trial database." In fact, col. 7, lines 28-31 in Pence, cited by the Examiner, merely describes

> "Step 95 compares the Sigma calculation to statistically significant thresholds. The thresholds are previously determined as being significant by the user."

One of ordinary skill in the art would not equate user defined thresholds with a user defined statistical model, as erroneously suggested by the Examiner. Moreover, after

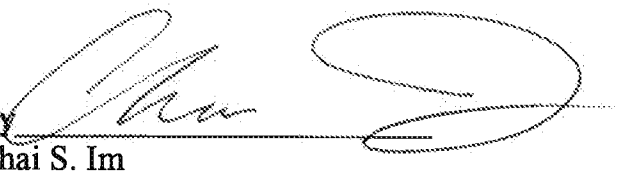
careful reading of Pence, applicant is unable to find any reference to clinical trial database, let alone using a user defined statistical model on the trial database. Applicant respectfully requests that the Examiner identify where in Pence it allegedly teaches "retrieving a user defined statistical model; and running the retrieved user defined statistical model on the trial database," as required in claim 11. The Examiner cannot simply change the principle of the operation of the reference or render the reference inoperable for its intended purpose to render the claims unpatentable.

In view of the foregoing, it is respectfully submitted that one of ordinary skill in the art, after reading and understanding Bardy, would not even turn to Pence – and if she did, she would not understand how or why Bardy's congestive heart monitoring system should be combined with Pence's manufacturing testing system. Even if such combination is made, the resulting combination will not teach or suggest the claimed invention because both Bardy and Pence teaches away from the claimed invention because they must know the data source (i.e., the identity of the patient or defective magnetic disk drive, thereby compromising the integrity of the blind). Therefore, the Examiner has again failed to establish a *prima facie* case of obviousness because these references independently or in combination thereof fails to solve the problem of continuously analyzing trial data of an ongoing blinded clinical trial for a statistically significant event to identify a potential positive or negative effect of a drug under study without suspending and compromising the integrity of the ongoing blinded clinical trial. Accordingly, Applicants respectfully request this rejection be withdrawn.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 50-0624, under Order No. NY-MSI 203-US from which the undersigned is authorized to draw.

Dated: April 8, 2009

Respectfully submitted,



By
Chai S. Im
Registration No.: 40,657
FULBRIGHT & JAWORSKI L.L.P.
666 Fifth Avenue
New York, New York 10103
(212) 318-3000
(212) 318-3400 (Fax)
Attorney for Applicant